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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,264	BARBER, ELIZABETH K.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5,8-14,16,18,22,23,37,38,41 and 42* is/are pending in the application.

4a) Of the above claim(s) __ is/are withdrawn from consideration.

5)☒ Claim(s) *22,23,41 and 42* is/are allowed.

6)☒ Claim(s) *1-5,8-14,16,18,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 10/12/04 has been acknowledged.

Claims 6-7, 15, 19-21, 24-36 and 39-40 are canceled.
Claims 41-42 are newly filed.
Claims 1-5, 8-14, 16-19, 22-23, 37-38 and, 41-42 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

Claims *1-5, 8-14, 16-18 and 37-38* are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the office action mailed on 05/10/04.

The scope of the instant invention encompasses a variant of SEQ ID NO:1 that comprising additional 10 to 150 consecutive nucleotides immediately upstream from SEQ ID N0: 1, wherein the polynucleotide is contained in SEQ ID N0: 2. The scope of invention as claimed further encompasses the nucleotide sequence of claim 1, wherein the DNA sequence of SEQ ID NO: 1 and the additional upstream nucleotides comprise a region of DNA that is homologous to or identical to a region of DNA comprising a

portion of the human dystrophin gene, wherein the DNA sequence of SEQ ID NO: 1 is inverted when compared to the same sequence of the human dystrophin DNA. In addition the scope of the polynucleotides as claimed encompasses a polynucleotides that encodes one or more polypeptides or proteins that binds to human CD33 protein. The scope of invention as claimed further encompasses a nucleotide sequence that hybridizes to the polynucleotide of claim 1. The scope of invention as claimed encompasses vectors and host cells comprising the nucleotide sequence of claim 1. The scope of invention as claimed further encompasses any regulatory DNA element comprising the nucleotide sequences of claim 1 or SEQ ID NO:1.

Response to arguments

The applicant argues that deletion of recitation of "substantial functional equivalent" in the claims as amended would obviate the instant rejection.

However, applicant's argument are found NOT persuasive because the scope of the instant invention encompasses a variant of SEQ ID NO:1 that comprising additional 10 to 150 consecutive nucleotides immediately upstream from SEQ ID N0: 1 which encompasses any and all variants of SEQ NO:1 contained in the SEQ ID NO:2. At best the specification discloses only one variant of the polynucleotide as claimed, which comprises polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1. The scope of invention as claimed encompasses addition of any 10-150 consecutive nucleotides, which would result in the variation of about 1-15% in the in the nucleotide sequences of SEQ ID NO:2. The specification fails to disclose any variant of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 or variant thereof explicitly or implicitly, wherein the variant is a functional variant of human dystrophin gene and is capable of binding to the human CD33 protein.

Applicant were referred to the guidelines for *Written Description Requirement* published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the

specification only teaches polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 but fails to disclose any variant of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 or a variant of SEQID NO:1 that has the functional property of a human dystrophin-like gene product and/or binds to CD33 explicitly or implicitly as putatively claimed by the applicant.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the nucleic acid variants (as claimed) has been defined only by a statement of function that broadly encompasses functional activity of dystrophin-like gene and/or binding to the human CD33 protein or any regulatory DNA element-like activity (i.e. promotor, binding site for any transcriptional factor), which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics.

Furthermore the variation as claimed (1-15%) would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted added or deleted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only

one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims *1-5, 8-14, 16-18 and 37-38* are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for human Apo-dystrophin-4 gene which comprises the nucleotide sequence of SEQ ID NO:2 that contains the nucleotide sequences of SEQ ID NO:1, does not reasonably provide enablement for a polynucleotides encoding any other variant of Apo-dystrophin-4 gene, wherein the Apo-dystrophin-4 gene comprises any and all functional equivalent of the polynucleotides (as claimed). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons of record as set forth in the office action mailed on 05/10/04.

Nature of Invention:

The instant invention is drawn to a variant of human dystrophin gene designated herein as Apo-dystrophin-4.

Breadth of Claims and Guidance Provided in the Specification

The scope of the instant invention encompasses a variant of SEQ ID NO:1 that comprising additional 10 to 150 consecutive nucleotides immediately upstream from SEQ ID N0: 1, wherein the polynucleotide is contained in SEQ ID N0: 2. The scope of invention as claimed further encompasses the nucleotide sequence of claim 1, wherein the DNA sequence of SEQ ID NO: 1 and the additional upstream nucleotides comprise a region of DNA that is homologous to or identical to a region of DNA comprising a portion of the human dystrophin gene, wherein the DNA sequence of SEQ ID NO: 1 is inverted when compared to the same sequence of the human dystrophin DNA. In addition the scope of the polynucleotides as claimed encompasses a polynucleotides that encodes one or more polypeptides or proteins that binds to human CD33 protein. The scope of invention as claimed further encompasses a nucleotide sequence that hybridizes to the polynucleotide of claim 1. The scope of invention as claimed

encompasses vectors and host cells comprising the nucleotide sequence of claim 1. The scope of invention as claimed further encompasses any regulatory DNA element comprising the nucleotide sequences of claim 1 or SEQ ID NO:1.

At best the specification discloses only a single variant of Apo-dystrophin-4 gene sequence, which comprises polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1. The specification discloses that the SEQ ID NO:1 is a 137bp long inversion sequence which begins at base pair location 860 and ends at base pair location 996 of the nucleotide sequences of SEQ ID NO:2 (996 bp) see Spec. page 3, para.1 fig-1). The specification further discloses that the nucleic acid sequence of SEQ ID NO:2 encodes a polypeptide which binds to human CD33 protein with low affinity.

State of Art and Predictability

The state of the art at the time of filing regarding dystrophin gene was such that the dystrophin gene is alternatively spliced throughout its coding sequence. Dystrophin is the largest known human gene. It extends over 3000 kb on the X chromosome and is transcribed into a 14-kb mRNA. The gene is composed of 79 exons that together account for only 0.6% of the sequence. Its main protein product, dystrophin, a member of the spectrin superfamily, is a rod-shaped 427-kDa protein. Three full-length dystrophin isoforms have been described, each controlled by a tissue-specific promoter. The muscle isoform is mainly expressed in skeletal muscle but also in smooth and cardiac muscles; brain dystrophin is specific for cortical neurons but can also be detected in heart and cerebellar neurons, while the Purkinje-cell type accounts for nearly all cerebellar dystrophin. Furthermore alternative splicing provides a means for dystrophin diversification. The 3' region of the gene undergoes alternative splicing resulting in tissue-specific transcripts in brain neurons, cardiac Purkinje fibres, and smooth muscle cells while 12 patterns of alternative splicing have been described in the 5' region of the gene in skeletal muscle (Sironi et al, FEBS Lett. 517:163-166, 2002, see page 163, col.1). Furthermore the alternative splicing events are differentially regulated in different organs and that deletions involving the same exons can determine diverse splicing behaviours in different patients or even in different tissues of the same

individual. In this view, allelic differences and tissue specificity in splicing factors should be regarded as possible determinants of disease expression and differential organ involvement (Sironi, page 166 col.2).

The myeloid restricted membrane glycoprotein CD33 is a member of the sialic acid-binding immunoglobulin-related lectin family, which mediates sialic acid-dependent cell interactions as a recombinant protein. The tyrosine phosphorylation of CD33 in myeloid cell lines is stimulated by cell surface cross-linking or by pervanadate, and inhibited by PP2, a specific inhibitor of Src family tyrosine kinases. The phosphorylated CD33 recruits both the protein-tyrosine phosphatases, SHP-1 and SHP-2, which modulate downstream signaling events associated with cell activation. The CD33 phosphorylation could be induced by ligand occupancy and subsequent clustering, which then trigger downstream signaling events in myeloid cells. Therefore the identification of CD33 ligand(s) is considered an important step in modulation of myeloid cell function via CD33 interaction especially in the treatment of acute myeloid leukemia (Taylor et al. J Biol Chem, 274(17):11505-11512, 1999, see abstract and page 11511 col.2 para.1) .

Response to arguments

The applicant argues that claim has been amended to delete recitation "substantial functional equivalent", which renders instant claims enabled to a person skilled in the art. The applicant argues that persons of skilled in the art are also provided with methods of expressing these sequences and determining whether apo-dystrophin-4 variants are expressed and whether these variants are able to bind to CD33. The applicant argues that such experiments such experimentation is routine in the art and would not require undue experimentation. The applicant argues that the evidence provided by the office that apo-dystrophin-4 is the result of alternative splicing comes from a post filing art (Sironi et al, 2002) that should not be used as evidence of non-enablement.

However, applicant's argument are found NOT persuasive because the scope of the instant invention encompasses a variant of SEQ ID NO:1 that comprising additional 10 to 150 consecutive nucleotides immediately upstream from SEQ ID N0: 1 which encompasses any and all variants of SEQ NO:1 contained in the SEQ ID NO:2. At best the specification discloses only one variant of the polynucleotide as claimed, which comprises polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1. The scope of invention as claimed encompasses addition of any 10-150 consecutive nucleotides, which would result in the variation of about 1-15% in the in the nucleotide sequences of SEQ ID NO:2. The specification fails to disclose any variant of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 or variant thereof explicitly or implicitly, wherein the variant is a functional variant of human dystrophin gene and is capable of binding to the human CD33 protein. Any variation as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo 1994 and Rudinger 1976).

In instant case the specification fails to disclose any other variant of SEQ ID NO:1 or SEQ ID NO:2 that is a substantial functional variant of human dystrophin gene and is also capable of binding to human CD33 protein which is consider the hallmark of acute myeloid leukemia. In addition the specification fails to disclose that polynucleotides of SEQ ID NO:1 encodes a protein or a polypeptide that is expressed on cell surface is vivo and is capable of binding to the human CD33 protein. Therefore considering the nature of dystrophin gene, which is known to be alternatively spliced, and complexities found in the modulation of CD33 mediated signal transduction by ligand binding, it is highly unpredictable that a substantial functional variants of the Apo-dystrophin-4 (as claimed) would bind to the human CD33 and/or have dystrophin gene like activity. Thus it would require an undue amount of experimentation to characterize

every possible variant for the claimed functional activity (i.e. binding to CD33 and modulation of CD33 mediated signal transduction or as another splice variants dystrophin gene which is express in tissue specific manner).

In addition screening of any and all natural and/or non-natural variants of Apo-dystrophin-4 gene product, wherein unknown numbers of amino acid sequences are added substituted and/or deleted is not considered routine in the art. Making and testing a point mutation is significantly different from the making and testing a gene product wherein unknown amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed functional activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Regarding claim 9 the applicant argues that polynucleotide sequences as claimed is necessary for the expression of the proteins of expressible from SEQ ID NO:2. The applicant further argues that this expression results from the suppression of stop codons in the to which the polynucleotide(s) of claim 9 are operatively linked.

However, applicant's arguments are found NOT persuasive because the scope of the polynucleotide as claimed encompasses a variant of SEQ ID NO:1 that comprising additional 10 to 150 consecutive nucleotides immediately upstream from SEQ ID N0: 1 which encompasses any and all variants of SEQ NO:1 contained in the SEQ ID NO:2 and contains any regulatory element. The scope of regulatory DNA element as claimed (claim 9) encompasses a DNA sequence encoding a promoter, which regulates the transcription of a gene. Furthermore the scope of regulatory DNA element as claimed encompasses a DNA sequence encoding any DNA binding site for

a transcriptional factor, which regulates the gene expression to which it is linked. Besides the presence of a start codon and a stop codon the specification as filed fails to disclose and that polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 contains a promoter or any transcriptional factor binding sites which is capable of regulating the expression of a gene or other DNA sequences to which it is operatively linked. The specification fails to provide a single working example which establishes that polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 are capable of regulating the expression of a gene or a DNA sequence to which it is operatively linked. Therefore considering the limited amount of disclosure one would have to engage in undue amount of experimentation to explore whether the polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 contains a promoter or any transcriptional factor binding site sequences which is capable of regulating the expression of a polynucleotide sequence of interest

With respect to claims 17 and 18 the applicant argues that invention as claimed is enabled, since one skilled in the art would be able to transduce hot cells in vivo created via a method of gene therapy.

However, applicant's arguments are found NOT persuasive. Considering the scope of invention, which encompasses a cell created by a method of gene therapy or making transgenic animal, the earlier office action suggested that amending instant claims to an isolated host cell would obviate this rejection. Given the broadest reasonable interpretation the scope of the "cell" as claimed encompasses any and all type of cells found in-vivo (i.e. hematopoietic stem cells, erythrocytes, leukocytes, neurons etc) transduction of which is considered highly unpredictable in-vivo. For example the earlier office action clearly states that it has been difficult to predict the efficiency and out come of transduced genes because various factors govern the expression and/or therapeutic potential of transduced genes in vivo. The transduction of target cells represents the first critical step in gene therapy, which not only depends upon the type of target cells but also on the choice and/or characteristics of delivery vectors. In addition, besides the limitations in gene transfer the problem to selectively target cells in vivo is still one of the most difficult obstacles to overcome. The viral

particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets. Thus making a host cell to produce recombinant protein (in-vivo), wherein the host cells is created by method of gene therapy or transgenic art are not considered routine in the art and without sufficient guidance the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Claims 17-18 drawn to an isolated host cell would obviate this rejection.

With respect to claims 37 and 38 the applicant argues that the nucleotide sequences of the invention may be used to treat conditions resulting from protein truncation. The applicant argues that the polynucleotide as claimed can be delivered to a muscle cell, which enables the invention of instant claims.

However, this is found unpersuasive because the invention as claimed encompasses a pharmaceutical composition for the treatment of a disorder in which protein truncation plays a part. The word " Pharmaceutical" means the administration of a medicinal drug of therapeutic value, which has a characteristic interaction in a body, in terms of its absorption, distribution, metabolism and excretion (see Pharmaceutical and related terms in Merriam Webster's Dictionary). The applicant fails to provide any guidelines for determining which individual need to be administered with the pharmaceutical composition as claimed. Furthermore, considering the scope of invention as claimed, it is unclear whether the disease would be the result of the loss of gene product or is the result of altered gene product function. It is even unclear whether the treatment of the disease associated with the gene as claimed would require increase or decrease in the expression of the gene product. At best the specification teaches that CD33 is a cell surface marker used to differentiate between acute lymphocytic and acute myelocytic leukemias. On the other hand the specification teaches that the regulation of CD33 including those elements to which it binds in vivo, is not fully understood and there is a need for investigation of this biological system (spec. page 1, lines 17-20). The specification teaches that apo-dystrophin-4 is a putative low-affinity ligand for CD33. The specification teaches that given the association of CD33

with leukemia, the invention provides a means to inactivate expression of a gene correlated with a disease phenotype (spec page 23, lines 1-6). However considering the unpredictability found in the treatment of leukemia the specification fails to disclose a single working example which establishes that the administration of a polynucleotide sequence comprising the polynucleotide sequences of SEQ ID NO:2 or SEQ ID NO:1, or any functional variants thereof would lead to the treatment of acute myelocytic leukemia. For example the specification even fails to disclose that low-affinity binding of apo-dystrophin-4 to CD33 is capable of modulating CD33 mediated signal transduction in the proliferation myeloid leukemic cells (see Taylor et al. J Biol Chem, 274(17):11505-11512, 1999). In addition the specification fails to disclose any other disease or disorder in which truncation of any protein play a part, wherein the disease is treatable by the administration of polynucleotide sequences of SEQ ID NO:2 or SEQ ID NO:1, or functional variants thereof. Under the law, the disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). Thus considering the applicant's disclosure the pharmaceutical composition comprising the claimed polynucleotide sequences is not found enabled for the treatment of any disease or disorder.

Conclusion

Claims *1-5, 8-14, 16-18 and 37-38* are rejected.

Claims 22-23 and 41-42 are allowable. The instant claims are free of prior art of record because the prior art does not teach or suggest the polynucleotide sequences of SEQ ID NO:2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If

attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
1/7/05